Practitioner's Docket No. IL-11138/LLNL010 *PATENT*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Letant et al.

Application No.: 10/677,395 Group No.: 1634
Filed: 10/01/2003 Examiner: Crow, Robert T.
For: FUNCTIONALIZED APERTURES FOR THE DETECTION OF CHEMICAL AND BIOLOGICAL MATERIALS

Mail Stop Appeal Briefs – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL OF APPEAL BRIEF
(PATENT APPLICATION--37 C.F.R. § 41.37)

1. Transmitted herewith, is the APPEAL BRIEF in this application, with respect to the Notice of Appeal filed on July 21, 2008.

2. STATUS OF APPLICANT

   This application is on behalf of a small entity. A statement was already filed.

3. FEE FOR FILING APPEAL BRIEF

   Pursuant to 37 C.F.R. § 41.20(b)(2), the fee for filing the Appeal Brief is:

small entity	$255.00
Appeal Brief fee due	**$255.00**

4. EXTENSION OF TERM

   The proceedings herein are for a patent application and the provisions of 37 C.F.R. § 1.136 apply.

   Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

5. TOTAL FEE DUE

   The total fee due is:

Appeal brief fee	$255.00
Extension fee (if any)	$0.00
TOTAL FEE DUE	**$255.00**

6. FEE PAYMENT

Authorization is hereby made to charge the amount of $255.00 to Deposit Account No. 50-1351 (Order No. LLNLP010).

7. FEE DEFICIENCY

If any additional extension and/or fee is required, and if any additional fee for claims is required, charge Deposit Account No. 50-1351 (Order No. LLNLP010).

Date: September 22, 2008

/Dominic M. Kotab/
Signature of Practitioner

Reg. No.: 42,762
Tel. No.: 408-971-2573
Customer No.: 78980

Dominic M. Kotab
Zilka-Kotab, PC
P.O. Box 721120
San Jose, CA 95172

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of Letant et al. Application No.: 10/677,395 Filed: 10/01/2003 For: FUNCTIONALIZED APERTURES FOR THE DETECTION OF CHEMICAL AND BIOLOGICAL MATERIALS	Group Art Unit: 1634 Examiner: CROW, Robert T. Attorney Docket No.: IL-11138/ LLNLP010 Date: September 22, 2008

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

ATTENTION: Board of Patent Appeals and Interferences

APPEAL BRIEF (37 C.F.R. § 41.37)

This brief is in furtherance of the Notice of Appeal, filed in this case on July 21, 2008.

The fees required under § 1.17, and any required petition for extension of time for filing this brief and fees therefor, are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

This brief contains these items under the following headings, and in the order set forth below (37 C.F.R. § 41.37(c)(i)):

I REAL PARTY IN INTEREST
II RELATED APPEALS AND INTERFERENCES
III STATUS OF CLAIMS
IV STATUS OF AMENDMENTS
V SUMMARY OF CLAIMED SUBJECT MATTER

VI GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

VII ARGUMENT

VIII CLAIMS APPENDIX

IX EVIDENCE APPENDIX

X RELATED PROCEEDING APPENDIX

The final page of this brief bears the practitioner's signature.

I REAL PARTY IN INTEREST (37 C.F.R. § 41.37(c)(1)(i))

The real party in interest in this appeal is Lawrence Livermore National Security, LLC.

II RELATED APPEALS AND INTERFERENCES (37 C.F.R. § 41.37(c) (1)(ii))

With respect to other prior or pending appeals, interferences, or related judicial proceedings that will directly affect, or be directly affected by, or have a bearing on the Board's decision in the pending appeal, there are no other such appeals, interferences, or related judicial proceedings.

A Related Proceedings Appendix is appended hereto.

III STATUS OF CLAIMS (37 C.F.R. § 41.37(c) (1)(iii))

A. TOTAL NUMBER OF CLAIMS IN APPLICATION

Claims in the application are: 1-24

B. STATUS OF ALL THE CLAIMS IN APPLICATION

1. Claims withdrawn from consideration: 10-11
2. Claims pending: 1-18
3. Claims allowed: None
4. Claims rejected: 1-9, 12-18
5. Claims cancelled: None

C. CLAIMS ON APPEAL

The claims on appeal are: 1-9, 12-18

IV STATUS OF AMENDMENTS (37 C.F.R. § 41.37(c)(1)(iv))

As to the status of any amendment filed subsequent to final rejection, no amendments were made.

V SUMMARY OF CLAIMED SUBJECT MATTER (37 C.F.R. § 41.37(c)(1)(v))

With respect to a summary of independent Claim 1, as described, inter alia, in paragraph [00012] and in Figure 3, an apparatus comprises a substrate having at least one aperture (14, Fig. 3) having a tapered portion (15, Fig. 3) with a top diameter greater than a bottom diameter (Fig. 3) and wherein in each said at least one aperture, the tapered portion (15, Fig. 3) of each said at least one aperture (14, Fig. 3) transitions into a cylindrical portion (16, Fig. 3) having a diameter equal to said bottom diameter of said tapered portion (Fig. 3). Referring to paragraph [00016], cross-linkers are attached to an inner wall of said at least one aperture (14, Fig. 3). Referring again to paragraph [00012], a macro-cyclic ring (17, Fig. 3), having a diameter substantially the same as the diameter of the cylindrical portion of said at least one aperture (paragraph [00012]), attached (17, Fig. 3) at or near the circumference of one end of the cylindrical portion of said at least one aperture (14, Fig. 3).

With respect to a summary of independent Claim 7, as described, inter alia, in paragraph [00012] and in Figure 3, an apparatus comprises a substrate having at least one aperture (14, Fig. 3) having a tapered portion (15, Fig. 3) with a top diameter greater than a bottom diameter (Fig. 3) and wherein in each said at least one aperture, the tapered portion (15, Fig. 3) of each said at least one aperture (14, Fig. 3) transitions into a cylindrical portion (16, Fig. 3) having a diameter equal to said bottom diameter of said tapered portion (Fig. 3). Referring to paragraph [00016], cross-linkers are attached to an inner wall of said at least one aperture (14, Fig. 3). With continued reference to paragraph [00016], antibodies or chemical functional groups are deposited around the inner walls of said at least one aperture (17, Fig. 3) or around the circumference of one end of said at least one aperture.

Of course, the above citations are merely examples of the above claim language and should not be construed as limiting in any manner.

VI GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL (37 C.F.R. § 41.37(c)(1)(vi))

Following, under each issue listed, is a concise statement setting forth the corresponding ground of rejection.

Issue # 1: Claims 7-8 and 16-18 have been rejected under 35 USC 102(b) as being anticipated by Branton et al. (WO 00/079257, hereinafter "Branton") as evidenced by Stryer (Biochemistry, 2nd ed., pp. 13-15 and 575 (1981)).

Issue # 2: Claims 1-5 and 12-15 have been rejected under 35 USC 103(a) as being unpatentable over Branton in view of Hoger (J. Polymer Sci. Part A; Poly. Chem., vol. 37, pp. 2685-2698 (1999), hereinafter "Hoger") as evidenced by Stryer.

Issue # 3: Claim 6 has been rejected under 35 USC 103(a) as being unpatentable over Branton in view of Hoger as evidenced by Stryer in yet further view of Go (US5104820).

Issue # 4: Claims 7 and 9 have been rejected under 35 USC 103(a) as being unpatentable over Branton in view of Go.

VII ARGUMENT (37 C.F.R. § 41.37(c)(1)(vii))

The claims of the groups noted below do not stand or fall together. In the present section, appellant explains why the claims of each group are believed to be separately patentable.

Issue # 1:

Claims 7-8 and 16-18 have been rejected under 35 USC 102(b) as being anticipated by Branton as evidenced by Stryer.

Group #1: Claims 7-8, 16-18

Claims 7-8, 16-18

In the final office action mailed April 11, 2008, claims 7-8 and 16-18 were rejected under 35 USC 102(b) as being anticipated by Branton as evidenced by Stryer.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Moreover, the identical invention must be shown in as complete detail as contained in the claim. *Richardson v. Suzuki Motor Co.* 868 F.2d 1226, 1236, 9USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

Appellants respectfully assert that the rejection of claim 7 is improper. Particularly, claim 7 requires a substrate having at least one aperture having a tapered portion with a top diameter greater than a bottom diameter and wherein in each said at least one aperture, the tapered portion of each said at least one aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion; cross-linkers attached to an inner wall of said at least one aperture; and antibodies or chemical functional groups deposited around the inner walls of said at least one aperture or around the circumference of one end of said at least one aperture.

The rejection asserts that Branton teaches chemical functional groups in the form of polymerases attached to Branton's substrate. However, Branton does not overtly disclose any functional groups. To meet this limitation, the rejection goes on to assert that [p]olymerases are

proteins, which comprise chemical functional groups as evidenced by Stryer." Appellants respectfully challenge this assertion on several grounds.

First, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros., supra.* It is clear that the claimed functional group limitation is not expressly described in Branton. Accordingly, it appears that the Examiner is stating that Branton inherently discloses functional groups by disclosing use of a polymerase. However, the logic of the rejection improperly requires a long chain of possibilities to support the inference that Branton's polymerases have functional groups. Particularly, from the art cited in the rejection, the best that the Examiner can assert is that the polymerase *may* be a protein, which *may* be *based on* an amino acid with a functional group. For the following reasons, this falls far short of showing the identical invention in as complete detail as contained in the claim, as required by *Richardson, supra.*

The rejection states that Stryer has been added merely for the teaching that proteins comprise functional groups and the claims remain rejected over the prior art of record. Particularly, it appears that the Examiner is asserting that polymerases are proteins, and then by extension that because proteins in general are based on amino acids, which may have functional groups, then proteins must have functional groups, and so the polymerases have functional groups.

However, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). Rather, to establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted, emphasis added). In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

The Examiner's assertion of inherency improperly relies on possibilities and probabilities, in violation of *In re Robertson, supra*. First, the Examiner has not shown that all amino acids have functional groups. Do some amino acids have functional groups, probably. Thus we have a first possibility, that amino acids have functional groups.

However, then consider that proteins are *reaction products* of amino acids. In other words, the base amino acid, which may or may not have a functional group, is then reacted with something to form a protein. Does the amino acid become something else? Yes, it becomes part of a protein. Does the amino acid retain its functional group, if it even has one? Possibly. Is the functional group still a functional group, or, now that the amino acid has reacted, is the functional group merely a nonfunctional branch of the protein, or even coupled to the other reactant? From the evidence of record, we do not know. As should now be apparent, the logic of the rejection relies on too many levels of possibilities to support the Examiner's assertion of inherency. Again, "[i]nherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson, supra.*

Moreover, Stryer does indicate that DNA polymerase I is an enzyme, but it is known that not all enzymes are proteins. Therefore, the rejection relies on the *possibility* that Branton's polymerase is not only the same as that in Stryer, *and also* that Stryer's DNA polymerase is a protein, *and yet further* that the protein is formed of amino acids that might have functional groups, *and even further that*, after all the processing necessary to convert the amino acids to the DNA polymerase, what might have been functional groups (if present) in the starting material are still functional groups rather than nonfunctional. As can be seen, the logic of the rejection relies on too many levels of possibilities to support the Examiner's assertion of inherency. Again, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert, supra*. Rather, inherency "may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson, supra.*

Nor can we simply take the Examiner's word for it. Again, to establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *In re Robertson, supra.*

For any of the foregoing reasons, the rejection of claim 7 is improper.

Claims 8 and 16-18 depend from claim 7, and therefore incorporate the limitations of claim 7. By virtue of their dependence, claims 8 and 16-18 are also believed to be allowable.

Issue # 2:

Claims 1-5 and 12-15 have been rejected under 35 USC 103(a) as being unpatentable over Branton in view of Hoger as evidenced by Stryer.

Group #1: Claims 1-5, 12-15

In the final office action mailed April 11, 2008, claims 1-5 and 12-15 were rejected under 35 USC 103(a) as being unpatentable over Branton in view of Hoger as evidenced by Stryer.

Appellants assert that the rejection is improper as failing the *Graham* test. The analysis of obviousness was set forth in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966). In order to establish a *prima facie* case of obviousness, three basic criteria must be met:

> First, there must be some *suggestion or motivation*, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the teachings of the references. Second, there must be a *reasonable expectation of success*. Finally, the prior art reference or combined references must teach or suggest *all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art*, and not based on applicant's disclosure (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991; *emphasis added*).

Appellants respectfully traverse the rejection as failing the *Graham* test. Specifically, the combination proposed in the rejection fails at least the first element of the *Graham* test.

First, the Examiner has failed to provide a reasonable motivation to make the proposed combination of features based on knowledge generally available to those skilled in the art and not provided by Applicants in the present disclosure.

> "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd.Pat.App.&Inter.1985).

Here, the Examiner has indicated that the motivation to combine the references is based on creating an apparatus having cyclical molecules therein that recognize guest molecules with precise complimentarity as taught by Hoger. However, as pointed out in detail below, neither reference teaches or suggests a macro-cyclic ring coupled to a solid substrate, much less at or near the circumference at one of the cylindrical portion of said at least one aperture, as claimed. Moreover, as discussed in detail below, one cannot simply combine random chemical structures and expect to have predictable results. Rather, as well known to those skilled in the chemical arts, one cannot accurately predict what the result of combining chemical structures will be, much less how the combination will perform, absent some teaching from one who has made and studied the combination.

Thus, the only conclusion that can be drawn is that the combination of features proposed in the rejection has been impermissibly drawn from Appellants' disclosure. Again, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure *In re Vaeck, supra.*

Next, the claimed invention would <u>not</u> have been predictable from the bare teachings of the prior art itself, or in knowledge generally known to those skilled in the art. The United States Supreme Court has acknowledged that there is no obviousness where the end result is unpredictable. In the recent case, *KSR International v. Teleflex Inc.*, 127 S.Ct. 1727 (2007), the Court's analysis included by implication the traditional notion that evidence of unpredictable results is evidence of non-obviousness. Therefore, even though the Court made sweeping changes to the obviousness analysis, it acknowledged that if the result of the proposed

modification or combination of features is unpredictable, there is no obviousness.

The courts have repeatedly stated that the chemical arts are, by their very nature, unpredictable. This case is no different. In the instant rejection, the Examiner proposes replacing Branton's polymerase with a cyclic molecule from Hoger. However, no showing has been made that such a substitution would work, and allow Branton's device to continue to operate. Rather, any result of such a substitution is truly unpredictable. For instance, will Branton's crosslinkers couple to Hoger's cyclical molecule? If so, what will the effect be on the resultant diameter of the cyclical molecule? Will it still allow passage of Branton's single strand of DNA? Further, would Branton's invention even work after such a substitution? (Note Branton's reliance on the "biological motor" created by polymerase and DNA at p. 36, line 23 to p. 38, line 30.)

The lack of any description of using cyclicals in Branton is further evidence that such a substitution was not predictable to those skilled in the art.

Moreover, the Examiner cites Scheme 4 on p. 2689 of Hoger for the proposition that the rings can be coupled to a support. However, as clearly shown on p. 2689 of Hoger and described in the first partial paragraph of col. 1 thereof, Scheme 4 is a synthesis process in which the precursors are attached to the solid support and, upon formation of the ring break free. Assuming the same result in Branton if Hoger's rings were employed therewith, the rings would appear to break free from Branton's aperture.

Further, a reading of the column on p. 2689 of Hoger directly under the drawing labeled "Scheme 4" indicates that the precursors coupled to the solid substrate are found to couple together, voiding the reaction that is to create the ring. Accordingly, whether one of Hoger's rings would form in Branton's aperture, or would couple with another of the precursors, adds yet another layer of unpredictability to the combination proposed by the Examiner.

Moreover, the Examiner has provided no showing of how such a ring could be coupled to Branton's aperture.

Because the result of the substitution proffered in the rejection is unpredictable, the claimed invention is not obvious. Accordingly, the rejection is improper.

In the Advisory Action mailed June 24, 2008, the Examiner notes that the arguments of counsel cannot take the place of evidence on the record. However, the burden does not lie on the Applicant to show the unpredictability of the results, but rather on the Examiner to show the predictability of the results with a high degree of certainty. In this case, he has not.

Expanding on the points above, even assuming arguendo that substitution of Branton's polymerase with Hoger's cyclic molecule would somehow render predictable results, such results would appear to render Branton's device inoperable, and thus unsatisfactory for its intended purpose.

Appellants therefore respectfully traverse the rejection of claim 1 as being improper, as the proposed modification would render Branton's invention unsatisfactory for its intended purpose. If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Particularly, the purpose of Branton's system is to analyze portions of a DNA strand as it moves through a hole. However, no showing has been made that Branton's device would be able to properly analyze DNA without the polymerase. Rather, the Examiner appears to be assuming that Hoger's cyclic molecule will perform the same function as the polymerase. [Appellants note that the Examiner has gone to great lengths to characterize a polymerase in the rejection of claim 7. Now it appears that the Examiner is asserting that the polymerase can be simply swapped with some other molecule.]

Further, if Hoger's cyclical molecule were added as suggested by the Examiner, the DNA strand might couple with the cyclical and stop. If so, Branton's device would no longer be able to analyze the strand in the hole, or any other strand in the sample, as Branton requires pulling the DNA strand through the aperture in sequential order. *See* Branton's Abstract. *See also* section G of the Office Action mailed April 11, 2008, where the Examiner states that Branton's device is "for evaluation a polymer molecule by causing the polymer molecule to move through an aperture in sequential order."

Moreover, the Examiner indicates in section F of the Office Action mailed April 11, 2008 that the Applicant's argument regarding the binding of the Branton's DNA strand to Hoger's cyclical if added to Hoger's aperture undermines Applicant's claim 11 (withdrawn). The Examiner is respectfully directed to claim 11, which recites "wherein said aperture is functionalized to bind to a specific biological or chemical moiety". Accordingly, Applicant's arguments do not undermine the embodiment of claim 11. Rather, the binding is an intended function of claim 11. In sharp contrast, such binding would indeed undermine Branton's device which, as set forth by the Examiner in section G of the Office Action mailed April 11, 2008, is

"for evaluation a polymer molecule by causing the polymer molecule to move through an aperture in sequential order."

For any one of the foregoing reasons, Branton's device would be rendered inoperable, in violation of *In re Gordon, supra*.

Accordingly, the rejection is improper for this reason as well.

Moreover, the rejection based on Hoger is not supported. The rejection, at Section 6, 7th paragraph, relies on Hoger' Scheme 4 to show macro-cyclic rings attached to solid supports. However, a reading of the column on Hoger p. 2689 directly under the drawing labeled "Scheme 4" indicates that Scheme 4 is not preferred. Particularly, the author notes that the precursors are found to couple together, voiding the reaction that is to create the ring. Further, at one point, the author refers to Scheme 4 as requiring "extreme approaches". *See* Hoger, p. 2689, first column.

In the Advisory Action mailed June 24, 2008, the Examiner appears to agree that Hoger Scheme 4 does not support the previous assertion that Hoger teaches macro-cyclic rings attached to solid supports in a manner that would meet the claim limitations. Particularly, the Examiner states in section C that "Applicant's citation is directed specifically to solid state reactions of precursors of macrocyclic ring, nor the preformed ring itself. Thus, Applicant's citation has no bearing on the attachment of a preformed ring onto a solid substrate after formation of the ring." (emphasis added) Appellants agree that Hoger Scheme 4 is directed to synthesis of the rings on a solid support, not to attachment of preformed rings onto a solid surface. Accordingly, because the Examiner admits that Hoger's Scheme 4 is a synthesis reaction that does not relate to attachment of preformed rings to a solid surface, the rejection improperly relies upon Hoger's Scheme 4 to show attachment of a ring to a solid support. (*See* Office Action mailed April 11, 2008, section 6, 7th paragraph.)

In any case, Hoger appears to teach away from coupling rings to a solid support. A *prima facie* case of obviousness may also be rebutted by showing that the art, in any material respect, teaches away from the claimed invention. *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997).

The rejection, at Section 6, 7th paragraph, relies on Hoger' Scheme 4 to show macro-cyclic rings attached to solid supports. However, a reading of the column on Hoger p. 2689 directly under the drawing labeled "Scheme 4" indicates that Scheme 4 is not preferred.

Particularly, the author notes that the precursors are found to couple together, voiding the reaction that is to create the ring. Further, at one point, the author refers to Scheme 4 as requiring "extreme approaches". *See* Hoger, p. 2689, first column.

Accordingly, because Hoger teaches away from a ring coupled to a solid support, the rejection violates the rule of *In re Geisler, supra*, and must be withdrawn.

For any of the foregoing reasons, reconsideration and allowance of claim 1 is respectfully requested.

Claims 2-5 and 12-15 depend from claim 1, and therefore incorporate the limitations of claim 1. By virtue of their dependence, claims 2-5 and 12-15 are also believed to be allowable. If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Reconsideration and allowance of claims 2-5 and 12-15 is respectfully requested.

Further, the deficiencies of the reliance on Stryer set forth above are incorporated by reference here for those claims for which the rejection relies on Stryer.

Issue # 3:

Claim 6 has been rejected under 35 USC 103(a) as being unpatentable over Branton in view of Hoger as evidenced by Stryer in yet further view of Go (US5104820).

Group #1: Claim 6

In the final office action mailed April 11, 2008, claim 6 was rejected under 35 USC 103(a) as being unpatentable over Branton in view of Hoger as evidenced by Stryer in yet further view of Go.

The rejection of claim 6 applies Branton and Hoger as for claim 1. Claim 6 depends from claim 1, and therefore the rejection suffers from the same deficiencies as set forth above with respect to claim 1. Because Go has merely been added to allegedly show the limitation of the

dependent claim, claim 6 is believed to be allowable over the combination proposed by the Examiner. Reconsideration and allowance of claim 6 is respectfully requested.

Issue # 4:

Claims 7 and 9 have been rejected under 35 USC 103(a) as being unpatentable over Branton in view of Go.

Group #1: Claims 7, 9

In the final office action mailed April 11, 2008, claims 7 and 9 were rejected under 35 USC 103(a) as being unpatentable over Branton in view of Go.

The rejection of claims 7 and 9 applies Branton as for claim 7, and therefore is erroneous for the same reasons as set forth above, namely that the rejection based on Branton is unsupported and/or improperly relies on official notice.

Reconsideration and allowance of claims 7 and 9 is respectfully requested.

In view of the remarks set forth hereinabove, all of the independent claims are deemed allowable, along with any claims depending therefrom.

VIII CLAIMS APPENDIX (37 C.F.R. § 41.37(c)(1)(viii))

The text of the claims involved in the appeal is set forth below:

1. An apparatus comprising:

a substrate having at least one aperture having a tapered portion with a top diameter greater than a bottom diameter and wherein in each said at least one aperture, the tapered portion of each said at least one aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion;

cross-linkers attached to an inner wall of said at least one aperture; and

a macro-cyclic ring, having a diameter substantially the same as the diameter of the cylindrical portion of said at least one aperture, attached at or near the circumference of one end of the cylindrical portion of said at least one aperture.

2. The apparatus of claim 1, wherein the substrate is chosen from the group consisting of glass, carbon, polymeric materials, and semiconductors.

3. The apparatus of claim 1, wherein the macro-cyclic ring has a rigid phenylethynyl backbone.

4. The apparatus of claim 1, wherein a biological or chemical probe is attached to the macro-cyclic ring such that the biological or chemical probe extends into and rests between at least a portion of the surfaces of the inner walls of the cylindrical portion of said aperture.

5. The apparatus of claim 4, wherein the biological probe comprises a single strand sequence of DNA.

6. The apparatus of claim 1, wherein the substrate

comprises a layer of Silicon Nitride, a layer of Silicon, a layer of Silicon Oxide, a layer of Silicon, and a layer of Silicon Nitride.

7. An apparatus comprising:

a substrate having at least one aperture having a tapered portion with a top diameter greater than a bottom diameter and wherein in each said at least one aperture, the tapered portion of each said at least one aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion;

cross-linkers attached to an inner wall of said at least one aperture; and

antibodies or chemical functional groups deposited around the inner walls of said at least one aperture or around the circumference of one end of said at least one aperture.

8. The apparatus of claim 7, wherein the substrate is chosen from the group consisting of glass, carbon, polymeric materials, and semiconductors.

9. The apparatus of claim 7, wherein the substrate comprises a layer of Silicon Nitride, a layer of Silicon, a layer of Silicon Oxide, a layer of Silicon, and a layer of Silicon Nitride.

10. A method comprising:

providing a substrate having at least one aperture having a tapered portion with a top diameter greater than the bottom diameter and wherein the tapered portion of the aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion; and

functionalizing said aperture to bind to a specific biological or chemical moiety.

11. A method comprising:

providing a substrate having at least one aperture having a tapered

portion with a top diameter greater than the bottom diameter and wherein the tapered portion of the aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion, wherein said aperture is functionalized to bind to a specific biological or chemical moiety; and

passing a sample through said aperture while simultaneously measuring the variation in ionic current across the depth of said aperture.

12. The apparatus of claim 1, wherein the macro-cyclic ring has at least one functional group coupled thereto.

13. The apparatus of claim 1, further comprising electrodes positioned to allow measurement of a current across the aperture.

14. The apparatus of claim 13, further comprising a device coupled to the electrodes for measuring the current across the aperture.

15. The apparatus of claim 14, wherein coupling of a biological or chemical material to a functional group coupled to the macrocyclic ring causes a change in the current across the aperture, the change being detectable by the device.

16. The apparatus of claim 7, further comprising electrodes positioned to allow measurement of a current across the aperture.

17. The apparatus of claim 16, further comprising a device coupled to the electrodes for measuring the current across the aperture.

18. The apparatus of claim 17, wherein coupling of a biological or chemical material to the antibodies or chemical functional groups causes a change in the current across the aperture, the change being detectable by the device.

IX EVIDENCE APPENDIX (37 C.F.R. § 41.37(c)(1)(ix))

There is no such evidence.

X RELATED PROCEEDING APPENDIX (37 C.F.R. § 41.37(c)(1)(x))

N/A

In the event a telephone conversation would expedite the prosecution of this application, the Examiner may reach the undersigned at (408) 971-2573. For payment of any additional fees due in connection with the filing of this paper, the Commissioner is authorized to charge such fees to Deposit Account No. 50-1351 (Order No. LLNLP010).

Respectfully submitted,

By: /Dominic M. Kotab/ Date: September 22, 2008
Dominic M. Kotab
Reg. No. 42,762

Zilka-Kotab, PC
P.O. Box 721120
San Jose, California 95172-1120
Telephone: (408) 971-2573
Facsimile: (408) 971-4660